51. (new) A kit for detecting a mismatch in any of a plurality of DNA duplexes of distinct nucleic acid sequence, comprising:

a first vector and a second vector, each such vector including an origin suitable for replication in a bacterial cell and a sequence that encodes a marker, said first and second vector marker encoding sequences differing from one another, said sequence difference capable of undergoing but not initiating in vivo mismatch repair.

52. (new) A bacterial host cell strain for detecting a mismatch in any of a plurality of DNA duplexes of distinct nucleic acid sequence, said host strain capable of mismatch repair and having an antibiotic marker cassette flanked by recombination sites.

REMARKS

In view of the above amendments and the following remarks, the Examiner is respectfully requested allow claims 27-52, the currently pending claims. Claims 1-26 have been canceled, without prejudice. No new matter is added.

Support for the language of the newly added claims is as follows. As stated in Claim 27, the hybridization of a plurality of DNA sequences in a single reaction may be found on page 16, line 12. The term, a "bacterial cell characteristic", is supported on page 9, line 23-24; and "mismatch corepair" of a marker on page 5, lines 3-4.

Support for the language of Claims 28-31, which recite, respectively, duplexes of 10, 100, 10,000 and 100,000 distinct nucleic acid sequences, may be found on page 16, lines 13-15.

The language of claims 32-36, specifying sources of nucleic acid sequences, may be found on page 14, lines 6-7, and line 21. The use of a coding region of a human gene is supported on page 2, lines 1-3.

Specific genes, as set forth in Claim 38, may be found on page 23, lines 21-24; and page 6, line 26. A mismatch in a single nucleotide, as recited in Claim 39, may be found on page 5, lines 24-25.

Marker genes, which include the use of a recombinase, as set forth in claims 41 and 42, is supported by page 9, lines 26-27; and the bacterial cell characteristics (claim 43-44) on page 9, lines 24-26.

The use of DNA sequences from a single individual, as recited in Claim 47-48, is supported in the specification on page 1, line 18 and page 14, line 20. The use of a pooled source of nucleic

acid strands (claim 49), is supported on page 34, line 26. The term "pooled from family members" (claim 50) is supported on page 35, line 27.

A kit for detecting a mismatch (Claim 51) is supported by the specification on page 23, lines 17-27. A bacterial strain having an antibiotic marker cassette flanked by recombination sites (Claim 52) is supported in the specification on page 9, lines 28-30.

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a Telephone Conference would expedite the prosecution of this application, he is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any other fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0815, order number UCSF-127CON.

Respectfully submitted,

Date: February 8, 2002

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APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

Replace the paragraph at page 1, lines 11-14 with the following rewritten paragraph:

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. Patent Application no. 09/271,055, filed March 17, 1999, which is a continuation-in-part of U.S. Patent Application no. 08/713,751, filed September 13, 1996; which claims priority to U.S. Provisional Patent Application no. 60/004,664, filed October 2, 1995.

IN THE CLAIMS

Cancel Claims 1-26.

Add the following new claims:

27. (new) A method of detecting a mismatch in any of a plurality of DNA duplexes of distinct nucleic acid sequence, said duplexes formed in a single hybridization reaction, comprising:

detecting, for any of said duplexes, an alteration in a bacterial cell characteristic, said alteration effected by the *in vivo* mismatch corepair of a marker that is present together with said duplex in a vector within said bacterial cell, said corepair being initiated by a mismatch in said duplex.

28. (new) The method of claim 27, wherein said plurality includes duplexes of at least 10 distinct nucleic acid sequences.

29. (new) The method of claim 28, wherein said plurality includes at least 100 duplexes of distinct nucleic acid sequence.

30. (new) The method of claim 29, wherein said plurality includes at least 10,000 duplexes of distinct nucleic acid sequence.

31. (new) The method of claim 29, wherein said plurality includes at least 100,000 duplexes of distinct nucleic acid sequence.

32. (new) The method of claim 27, wherein said plurality includes nucleic acid sequences derived from a prokaryote.

33. (new) The method of claim 27, wherein said plurality includes nucleic acid sequences derived from a virus.

34. (new) The method of claim 27, wherein said plurality includes nucleic acid sequences derived from a eukaryote.

35. (new) The method of claim 34, wherein said eukaryote is a mammal.

36. (new) The method of claim 35, wherein said mammal is a human.

37. (new) The method of claim 36, wherein said plurality includes nucleic acid sequences derived from the coding region of a human gene.

38. (new) The method of claim 37, wherein said human gene is selected from the group consisting of: hemoglobin, dystrophin, BRCA1, BRCA2, CFTR, factor VIII, factor IX, oncogenes, tumor suppressors, and genes on human chromosome 21.

39. (new) The method of claim 27, wherein said mismatch in said duplex is a single nucleotide polymorphism.

40. (new) The method of claim 27, wherein said marker is inactivated by said *in vivo* mismatch corepair.

41. (new) The method of claim 27, wherein said marker is a recombinase.

42. (new) The method of claim 41, wherein said recombinase is Cre recombinase.

43. (new) The method of claim 27, wherein said bacterial cell characteristic is selected from the group consisting of: cell color, luminescence, antibiotic sensitivity, and antibiotic resistance.

44. (new) The method of claim 41, wherein mismatch corepair of said recombinase alters

said bacterial cell's antibiotic resistance or sensitivity.

45. (new) The method of claim 27, further comprising the antecedent step of forming said plurality of DNA duplexes by annealing first nucleic acid strands, said first strands including at least one nucleic acid sequence, to second nucleic acid strands, said second strands including a plurality of distinct nucleic acid sequences.

46. (new) The method of claim 45, wherein said plurality of second nucleic acid strands are derived from a common source.

47. (new) The method of claim 46, wherein said common source is genomic DNA from a single individual.

48. (new) The method of claim 46, wherein said common source is cDNA from a single individual.

49. (new) The method of claim 45, wherein said plurality of second nucleic acid strands are derived from a pooled source.

50. (new) The method of claim 49, wherein said source is pooled from family members.

51. (new) A kit for detecting a mismatch in any of a plurality of DNA duplexes of distinct nucleic acid sequence, comprising:

a first vector and a second vector, each such vector including an origin suitable for replication in a bacterial cell and a sequence that encodes a marker, said first and second vector marker encoding sequences differing from one another, said sequence difference capable of undergoing but not initiating in vivo mismatch repair.

52. (new) A bacterial host cell strain for detecting a mismatch in any of a plurality of DNA duplexes of distinct nucleic acid sequence, said host strain capable of mismatch repair and having an antibiotic marker cassette flanked by recombination sites.